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Bescheinigung | Certificate | Attestation

Die angehefteten Unterlagen stimmen mit der ursprünglich eingereichten Fassung der auf dem nächsten Blatt bezeichneten internationalen Patentanmeldung überein.

The attached documents are exact copies of the international patent application described on the following page, as originally filed.

Les documents fixés à cette attestation sont conformes à la version initialement déposée de la demande de brevet international spécifiée à la page suivante.

Den Haag, den
The Hague,
La Haye, le 09 FEB 2004

Der Präsident des Europäischen Patentamts
Im Auftrag
For the President of the European Patent Office
Le Président de l'Office européen des brevets
p.o.

B. GATINET
(0)70/3402181

Patentanmeldung Nr.
Patent application no.
Demande de brevet n° PCT/EP 02/11409

Blatt 2 der Bescheinigung
Sheet 2 of the certificate
Page 2 de l'attestation

Anmeldung Nr.:
Application no.: PCT/EP 02/11409
Demande n°:

Anmelder:
Applicant(s):
Demandeur(s):
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2. AISSAOUI, Hamed - Wittenheim, France (US only)
3. CLOZEL, Martine - Binningen, Switzerland (US only)

Bezeichnung der Erfindung:
Title of the invention:
Titre de l'invention: SULFONYLAMINO-ACETIC ACID DERIVATIVES

Anmeldetag:
Date of filing: 11 October 2002 (11.10.2002)
Date de dépôt:

In Anspruch genommene Priorität(en)
Priority(ies) claimed
Priorité(s) revendiquée(s)

Staat: State: Pays:	Tag: Date: Date:	Aktenzeichen: File no. Numéro de dépôt:

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Designation of contracting states : See Form PCT/RO/101 (enclosed)
Désignation d'états contractants : Voir Formulaire PCT/RO/101 (ci-joint)

Bemerkungen:
Remarks:
Remarques:

Further applicants:

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PCT REQUEST Act 31/OR4

Original (for **SUBMISSION**) - printed on 08.10.2002 02:58:53 PM

0	**For receiving Office use only**	
0-1	International Application No.	PCT/EP 0 2 / 1 1 4 0 9
0-2	International Filing Date	11. 10. 2002 11 OCT 2002
0-3	Name of receiving Office and "PCT International Application"	EUROPEAN PATENT OFFICE PCT INTERNATIONAL APPLICATION

0-4	**Form - PCT/RO/101 PCT Request**	
0-4-1	Prepared using	PCT-EASY Version 2.92 (updated 01.06.2002)
0-5	**Petition** The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	
0-6	**Receiving Office (specified by the applicant)**	European Patent Office (EPO) (RO/EP)
0-7	**Applicant's or agent's file reference**	Act 31/OR4
I	**Title of invention**	SULFONYLAMINO-ACETIC ACID DERIVATIVES
II	**Applicant**	
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III-3-7	State of residence	CH
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III-4-7	State of residence	DE
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III-5-7	State of residence	FR

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III-6	**Applicant and/or inventor**	
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III-6-7	State of residence	CH
IV-1	**Agent or common representative; or address for correspondence** The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	agent
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IV-1-3	Telephone No.	+41 61 713 1560
IV-1-4	Facsimile No.	+41 61 713 15 61
IV-1-5	e-mail	hofmanndrd@bluewin.ch
V	**Designation of States**	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE BG CH&LI CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT

V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&LI CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
V-5	**Precautionary Designation Statement** In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	**Exclusion(s) from precautionary designations**	NONE
VI	**Priority claim**	NONE
VII-1	**International Searching Authority Chosen**	European Patent Office (EPO) (ISA/EP)

VIII	**Declarations**	Number of declarations	
VIII-1	Declaration as to the identity of the inventor	-	
VIII-2	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	-	
VIII-3	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	-	
VIII-4	Declaration of inventorship (only for the purposes of the designation of the United States of America)	-	
VIII-5	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	-	

IX	**Check list**	number of sheets	electronic file(s) attached
IX-1	Request (including declaration sheets)	5	-
IX-2	Description	41	-
IX-3	Claims	5	-
IX-4	Abstract	1	EZABST00.TXT
IX-5	Drawings	0	-
IX-7	TOTAL	52	

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	Accompanying items	paper document(s) attached	electronic file(s) attached
IX-8	Fee calculation sheet	✓	-
IX-11	Copy of general power of attorney	reference no. 40835	-
IX-17	PCT-EASY diskette	-	Diskette
IX-19	**Figure of the drawings which should accompany the abstract**		
IX-20	**Language of filing of the international application**	English	
X-1	**Signature of applicant, agent or common representative**	Hofmann, Dieter	
X-1-1	Name (LAST, First)	HOFMANN, Dieter	

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10-1	**Date of actual receipt of the purported international application**	11. 10. 02	11 OCT 2002
10-2	**Drawings:**		
10-2-1	Received		
10-2-2	Not received		
10-3	**Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application**		
10-4	**Date of timely receipt of the required corrections under PCT Article 11(2)**		
10-5	**International Searching Authority**	ISA/EP	
10-6	**Transmittal of search copy delayed until search fee is paid**		

FOR INTERNATIONAL BUREAU USE ONLY

11-1	**Date of receipt of the record copy by the International Bureau**	

ACTELION 31/OR4

Sulfonylamino-acetic acid Derivatives

The present invention relates to novel sulfonylamino-acetic acid derivatives of the general formula (I) and their use as pharmaceuticals. The invention also concerns related aspects including pharmaceutical compositions containing one or more compounds of formula I, and especially their use as orexin receptor antagonists.

The orexins (hypocretins) comprise two neuropeptides produced in the hypothalamus: the orexin A (OX-A) (a 33 aminoacid peptide) and the orexin B (OX-B) (a 28 aminoacid peptide) (Sakurai T. *et al.*, **Cell**, 1998, 92, 573-585). Orexins are found to stimulate food consumption in rats suggesting a physiological role for these peptides as mediators in the central feedback mechanism that regulates feeding behavior (Sakurai T. *et al.*, **Cell**, 1998, 92, 573-585). On the other hand, it was also proposed that orexins regulate states of sleep and wakefulness opening potentially novel therapeutic approaches for narcoleptic patients (Chemelli R.M. *et al.*, **Cell**, 1999, 98, 437-451). Two orexin receptors have been cloned and characterized in mammals which belong to the G-protein coupled receptor superfamily (Sakurai T. *et al.*, **Cell**, 1998, 92, 573-585), the orexin-1 receptor (OX_1) which is selective for OX-A and the orexin-2 receptor (OX_2) which is capable to bind OX-A as well as OX-B.

Orexin receptors are found in the mammalian host and may be responsible for many pathologies including, but not limited to, depression; anxiety; addictions; obsessive compulsive disorder; affective neurosis; depressive neurosis; anxiety neurosis; dysthymic disorder; behaviour disorder; mood disorder; sexual dysfunction; psychosexual dysfunction; schizophrenia; manic depression; delerium; dementia; severe mental retardation and dyskinesias such as Huntington's disease and Tourette syndrome; feeding disorders such as anorexia, bulimia, cachexia and obesity; diabetes; appetite/taste disorders; vomiting/nausea; asthma; cancer; Parkinson's disease; Cushing's syndrome/disease; basophil adenoma; prolactinoma; hyperprolactinemia; hypopituitarism; hypophysis tumor/adenoma; hypothalamic diseases; inflammatory bowel disease; gastric diskinesia; gastric ulcus; Froehlich's syndrome; adrenohypophysis disease; hypophysis disease; pituitary growth hormone; adrenohypophysis hypofunction; adrenohypophysis hyperfunction; hypothalamic hypogonadism; Kallman's syndrome (anosmia, hyposmia);

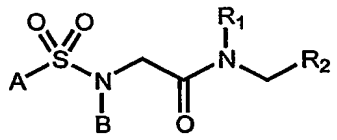
functional or psychogenic amenorrhea; hypopituitarism; hypothalamic hypothyroidism; hypothalamic-adrenal dysfunction; idiopathic hyperprolactinemia; hypothalamic disorders of growth hormone deficiency; idiopathic growth deficiency; dwarfism; gigantism; acromegaly; disturbed biological and circadian rhythms; sleep disturbances associated with deseases such as neurological disorders, neuropathic pain and restless leg syndrome; heart and lung diseases, acute and congestive heart failure; hypotension; hypertension; urinary retention; osteoporosis; angina pectoris; myocardinal infarction; ischaemic or haemorrhagic stroke; subarachnoid haemorrhage; ulcers; allergies; benign prostatic hypertrophy; chronic renal failure; renal disease; impaired glucose tolerance; migraine; hyperalgesia; pain; enhanced or exaggerated sensitivity to pain such as hyperalgesia, causalgia, and allodynia; acute pain; burn pain; atypical facial pain; neuropathic pain; back pain; complex regional pain syndrome I and II; arthritic pain; sports injury pain; pain related to infection e.g. by HIV; post-chemotherapy pain; post-stroke pain; post-operative pain; neuralgia; conditions associated with visceral pain such as irritable bowel syndrome, migraine and angina; urinary bladder incontinence e.g. urge incontinence; tolerance to narcotics or withdrawal from narcotics; sleep disorders; sleep apnea; narcolepsy; insomnia; parasomnia; jet-lag syndrome; and neurodegerative disorders including nosological entities such as disinhibition-dementia-parkinsonism-amyotrophy complex; pallido-ponto-nigral degeneration epilepsy; seizure disorders and other diseases related to orexin.

Up to now some low molecular weight compounds are known which have a potential to antagonise either specifically OX_1 or OX_2, or both receptors at the same time. In WO 99/09024, WO 99/58533, WO 00/47576, WO 00/47577 and WO 00/47580 formerly SmithKline Beecham reported phenylurea, phenylthiourea and cinnamide derivatives as OX_1 selective antagonists. More recently WO 01/85693 from Banyu Pharmaceuticals has been published wherein N-acyltetrahydroisoquinoline derivatives are disclosed. 2-Amino-methylpiperidine (WO 01/96302) and 3-aminomethylmorpholine (WO 02/44172) derivatives have been suggested by formerly SmithKline Beecham as orexin receptor antagonists. International patent applications WO 01/68609 and WO 20/51838 disclose 1,2,3,4-tetrahydroisoquinoline and novel benzazepine derivatives as orexin receptor antagonists. The novel compounds of the present invention belong to an entirely different class of low molecular weight compounds as compared to all prior art orexin receptor antagonists so far published.

The present invention comprises sulfonylamino-acetic acid derivatives which are non-peptide antagonists of the human orexin receptors, in particular the human orexin-2 receptor. These compounds, therefore, are of potential use in the treatment of disturbed homeostasis and eating disorders (e.g. bulimia, obesity, food abuse, compulsive eating) or irritable bowel syndrome, as well as disturbed sleep/wake schedule, sleep disorders (e.g. insomnias, apneas, dystonias) or stress-related diseases (e.g. anxiety, mood and blood pressure disorders).

WO 00/50391 discloses certain sulfonamide derivatives as modulators of the production of amyloid β-protein. WO 02/32864 discloses certain sulfanilide derivatives useful in the treatment of diseases mediated by oxytocin and/or vasopressin.

The present invention relates to novel sulfonylamino-acetic acid derivatives of the general formula (I).



Formula (I)

wherein:

A represents 4-ethylphenyl-, 4-isopropylphenyl-, 4-*tert.*-butylphenyl-, 2-methylphenyl-, 3-methylphenyl-, 3-fluorophenyl-, 2-chlorophenyl-, 3-chlorophenyl-, 4-bromophenyl-, 2-trifluoromethylphenyl-, 3-trifluoromethylphenyl-, 3-chloro-4-methylphenyl-, 2-methoxy-4-methylphenyl-, 3,4-difluorophenyl-, phenylethenyl-, 1-naphthyl-, 2-naphthyl-, 6-bromo-5-chloro-pyridin-3-yl or 8-quinolinyl-;

B represents a phenyl or 6-membered heteroaryl group, which groups are unsubstituted or independently mono- or di- substituted with cyano, halogen, hydroxy, lower alkyl, hydroxy lower alkyl, amino lower alkyl, aminocarbonyl lower alkyl, sulfonylamino lower alkyl, lower alkenyl, lower alkoxy, trifluoromethyl, trifluoromethoxy, cycloalkyloxy, aryloxy, aralkyloxy, heterocyclyloxy, heterocyclyl lower alkyloxy, amino, aminocarbonyl or

sulfonylamino; or a cyclohexyl, 3-piperidinyl or 4-piperidinyl group, which groups are unsubstituted or mono-substituted with hydroxy, lower alkyl, hydroxy lower alkyl, aminocarbonyl lower alkyl, sulfonylamino lower alkyl, amino, aminocarbonyl or sulfonylamino;

with the proviso that in case A represents 2-methylphenyl- or 4-bromophenyl the phenyl ring as represented by B is substituted;

R^1 represents lower alkyl;

R^2 represents lower alkyl, lower alkenyl, hydroxy lower alkyl, amino lower alkyl, sulfonylamino lower alkyl, cycloalkyl; an unsubstituted or mono- or di-substituted phenyl group substituted independently with cyano, halogen, hydroxy, lower alkyl, lower alkoxy, cycloalkyloxy, amino, aminocarbonyl or sulfonylamino; an unsubstituted or mono- or di-substituted five- or six-membered heteroaryl group substituted independently with cyano, halogen, hydroxy, lower alkyl, lower alkoxy, cycloalkyloxy, amino, aminocarbonyl or sulfonylamino;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

In the present description the term "lower alkyl", alone or in combination, means a straight-chain or branched-chain alkyl group with 1-5 carbon atoms as for example methyl, ethyl, propyl, isopropyl, butyl, sec.-butyl, tert.-butyl, isobutyl and the isomeric pentyls.

The term "lower alkenyl" means a straight-chain or branched-chain alkenyl group with 2 to 5 carbon atoms, preferably allyl and vinyl.

The term "lower alkoxy", alone or in combination, means a group of the formula lower alkyl-O- in which the term "lower alkyl" has the previously given significance, such as methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, isobutoxy, sec-butoxy and tert-butoxy, preferably methoxy and ethoxy.

The term "cycloalkyl", alone or in combination, means a cycloalkyl ring with 3 to 6 carbon atoms. Examples of C_3-C_6 cycloalkyl are cyclopropyl, cyclobutyl, cyclopentyl,

The term "cycloalkyl", alone or in combination, means a cycloalkyl ring with 3 to 6 carbon atoms. Examples of C_3-C_6 cycloalkyl are cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, preferably cyclopropyl, cyclohexyl and particularly cyclohexyl or lower alkyl substituted cycloalkyl which may preferably be substituted with lower alkyl such as methyl-cyclopropyl, dimethyl-cyclopropyl, methyl-cyclobutyl, methyl-cyclopentyl, methyl-cyclohexyl or dimethyl-cyclohexyl.

The term "aryl" means a phenyl or naphthyl group which optionally carries one or more substituents, preferably one or two substituents, each independently selected from cyano, halogen, hydroxy, lower alkyl, lower alkenyl, lower alkoxy, lower alkenyloxy, trifluoromethyl, trifluoromethoxy, amino, or carboxy.

The term "aralkyl" means a lower alkyl group as previously defined in which one hydrogen atom has been replaced by an aryl group as previously defined.

The term "heterocyclyl" means a 5- to 10-membered monocyclic or bicyclic ring, which may be saturated, partially unsaturated or aromatic containing for example 1, 2 or 3 heteroatoms selected from oxygen, nitrogen and sulphur which may be the same or different. Examples of such heterocyclyl groups are pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, quinolyl, isoquinolyl, thienyl, thiazolyl, isothiazolyl, furyl, imidazolyl, pyrazolyl, pyrrolyl, indazolyl, indolyl, isoindolyl, isoxazolyl, oxazolyl, quinoxalinyl, phthalazinyl, cinnolinyl, dihydropyrrolyl, pyrrolidinyl, isobenzofuranyl, tetrahydrofuranyl, dihydropyranyl. The heterocyclyl group may have up to 5, preferably 1, 2 or 3 optional substituents. Examples of suitable substituents include halogen, lower alkyl, amino, nitro, cyano, hydroxy, lower alkoxy, carboxy and lower alkyloxy-carbonyls.

The term "6-membered heteroaryl group" means a pyridyl, pyrimidinyl, pyrazinyl or a pyridazinyl group.

The term "5-membered heteroaryl group" means a pyrrolyl, furyl, thienyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl or thiadiazolyl group.

The term "amino" in terms like "amino", "amino lower alkyl", "aminocarbonyl" or "aminocarbonyl lower alkyl" represents a NH_2-, NHR^3- or a NR^3R^4-group. R^3 and R^4 are lower alkyl groups, which might be equal or different.

The term "sulfonylamino" in terms like "sulfonylamino" or "sulfonylaminoalkyl" represents a $R^5S(O)_2NR^3$-group. R^5 represents a lower alkyl group, a phenyl group, a 6-membered heteroaryl group or a 5-membered heteroaryl group.

A preferred group of compounds of formula (I) are those in which B, R^1 and R^2 have the meaning given above and A represents a 4-ethylphenyl group;
and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

Another preferred group of compounds of formula (I) are those in which B, R^1 and R^2 have the meaning given above and A represents a 4-isopropylphenyl group;
and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

Another preferred group of compounds of formula (I) are those in which B, R^1 and R^2 have the meaning given above and A represents a 4-*tert.*-butylphenyl group;
and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

Another preferred group of compounds of formula (I) are those in which B, R^1 and R^2 have the meaning given above and A represents a 2-methylphenyl group;
and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

Another preferred group of compounds of formula (I) are those in which B, R^1 and R^2 have the meaning given above and A represents a 3-methylphenyl group;
and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and

the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

Another preferred group of compounds of formula (I) are those in which B, R^1 and R^2 have the meaning given above and A represents a 3-chloro-4-methylphenyl group;
and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

Another preferred group of compounds of formula (I) are those in which B, R^1 and R^2 have the meaning given above and A represents a 2-naphthyl group;
and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

Examples of preferred compounds of formula (I) are:
N,N-Diethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide;
N,N-Diethyl-2-[(toluene-3-sulfonyl)-p-tolyl-amino]-acetamide;
N,N-Diethyl-2-[(4-ethyl-benzenesulfonyl)-p-tolyl-amino]-acetamide;
N,N-Diethyl-2-[(4-isopropyl-benzenesulfonyl)-p-tolyl-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-phenyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-cyclohexyl-amino]-*N,N*-diethyl-acetamide;
2-[(3-Chloro-4-methyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
N,N-Diethyl-2-[(naphthalene-2-sulfonyl)-p-tolyl-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-o-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-methyl-cyclohexyl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(3-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
N-Benzyl-*N*-ethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-dipropyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
N-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-pyridin-4-ylmethyl-acetamide;
N,N-Diethyl-2-[phenyl-(toluene-3-sulfonyl)-amino]-acetamide;
N,N-Diethyl-2-[(4-ethyl-benzenesulfonyl)-phenyl-amino]-acetamide;
N,N-Diethyl-2-[(3-fluoro-benzenesulfonyl)-p-tolyl-amino]-acetamide;
N,N-Diethyl-2-[((E)-2-phenyl-ethenesulfonyl)-p-tolyl-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-phenyl-amino]-*N*-ethyl-*N*-methyl-acetamide;
2-[(2-Chloro-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(3-Chloro-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(3,4-Difluoro-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
N,N-Diethyl-2-[(naphthalene-2-sulfonyl)-phenyl-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-methyl-acetamide;
N,N-Dipropyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide;
N,N-Diethyl-2-[(2-methoxy-4-methyl-benzenesulfonyl)-p-tolyl-amino]-acetamide;
N,N-Diethyl-2-[(quinoline-8-sulfonyl)-p-tolyl-amino]-acetamide;
N,N-Diethyl-2-[p-tolyl-(2-trifluoromethyl-benzenesulfonyl)-amino]-acetamide;
N,N-Diethyl-2-[p-tolyl-(3-trifluoromethyl-benzenesulfonyl)-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-ethyl-phenyl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-(2-hydroxy-ethyl)-acetamide;
2-[(4-Bromo-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-cyclohexyl-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-trifluoromethyl-phenyl)-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-(4-trifluoromethyl-phenyl)-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-(3-methoxy-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-(4-methoxy-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;

2-[(6-Bromo-5-chloro-pyridine-3-sulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-(2-chloro-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;

N,N-Diethyl-2-[(6-methoxy-pyridin-3-yl)-(toluene-2-sulfonyl)-amino]-acetamide;

N-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-(6-methoxy-pyridin-3-yl)-amino]-*N*-ethyl-acetamide;

N,N-Diethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-(6-methoxy-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;

N-Benzyl-*N*-ethyl-2-[(6-methoxy-pyridin-3-yl)-(toluene-2-sulfonyl)-amino]-acetamide;

N-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide;

N-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-ethyl-acetamide;

N-Benzyl-*N*-ethyl-2-[(6-methoxy-pyridin-3-yl)-(naphthalene-2-sulfonyl)-amino]-acetamide;

N-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(naphthalene-2-sulfonyl)-amino]-acetamide;

Examples of particularly preferred compounds of formula (I) are:

N,N-Diethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide;

N,N-Diethyl-2-[(toluene-3-sulfonyl)-p-tolyl-amino]-acetamide;

N,N-Diethyl-2-[(4-ethyl-benzenesulfonyl)-p-tolyl-amino]-acetamide;

N,N-Diethyl-2-[(4-isopropyl-benzenesulfonyl)-p-tolyl-amino]-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-phenyl-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-cyclohexyl-amino]-*N,N*-diethyl-acetamide;

2-[(3-Chloro-4-methyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;

N,N-Diethyl-2-[(naphthalene-2-sulfonyl)-p-tolyl-amino]-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-o-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-methyl-cyclohexyl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(3-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
N-Benzyl-*N*-ethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-dipropyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
N-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-pyridin-4-ylmethyl-acetamide;
N,N-Diethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(6-methoxy-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
N-Benzyl-*N*-ethyl-2-[(6-methoxy-pyridin-3-yl)-(toluene-2-sulfonyl)-amino]-acetamide;
N-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide;
N-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-ethyl-acetamide;
N-Benzyl-*N*-ethyl-2-[(6-methoxy-pyridin-3-yl)-(naphthalene-2-sulfonyl)-amino]-acetamide;
N-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(naphthalene-2-sulfonyl)-amino]-acetamide;

The present Invention encompasses physiologically usable or pharmaceutically acceptable salts of compounds of formula (I). This encompasses salts with physiologically compatible mineral acids such as hydrochloric acid, sulphuric or phosphoric acid; or with

organic acids such as formic acid, methanesulphonic acid, acetic acid, trifluoroacetic acid, citric acid, fumaric acid, maleic acid, tartaric acid, succinic acid or salicylic acid and the like. The compounds of formula (I) which are acidic can also form salts with physiologically compatible bases.

Examples of such salts are alkali metal, alkali earth metal, ammonium and alkylammoniumsalts such as Na, K, Ca or tetraalkylammonium salt. The compounds of formula (I) can also be present in the form of a zwitterion.

The present invention encompasses also solvation complexes of compounds of general formula (I). The solvation can be effected in the course of the manufacturing process or can take place separately, e.g. as a consequence of hygroscopic properties of an initially anhydrous compound of general formula (I).

The present invention further encompasses different morphological forms, e.g. crystalline forms, of compounds of general formula (I) and their salts and solvation complexes. Particular heteromorphs may exhibit different dissolution properties, stability profiles, and the like, and are all included in the scope of the present invention.

The compounds of formula (I) might have one or several asymmetric centres and can be present in the form of optically pure enantiomers, mixtures of enantiomers such as, for example, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates or mixtures of diastereoisomeric racemates and the meso-forms.

Preferred compounds as described above have IC_{50} values below 1000 nM, particularly preferred compounds have IC_{50} values below 100 nM which have been determined with the FLIPR (Fluorometric Imaging Plates Reader) method described in the beginning of the experimental section.

The compounds of formula (I) and their pharmaceutically usable salts can be used for the treatment of diseases or disorders where an antagonist of a human orexin receptor is required such as obesity, diabetes, prolactinoma, narcolepsy, insomnia, sleep apnea, parasomnia, depression, anxiety, addictions, schizophrenia and dementia.

The compounds of formula (I) and their pharmaceutically usable salts are particularly useful for the treatment of disturbed homeostasis and eating disorders (e.g. bulimia, obesity, food abuse, compulsive eating) or irritable bowel syndrome, as well as disturbed sleep/wake schedule, sleep disorders (e.g. insomnias, apneas, dystonias) or stress-related diseases (e.g. anxiety, mood and blood pressure disorders).

The compounds of formula (I) and their pharmaceutically usable salts can be used as medicament (e.g. in the form of pharmaceutical preparations). The pharmaceutical preparations can be administered enterally, such as orally (e.g. in the form of tablets, coated tablets, dragées, hard and soft gelatine capsules, solutions, emulsions or suspensions), nasally (e.g. in the form of nasal sprays) or rectally (e.g. in the form of suppositories). However, the administration can also be effected parenterally, such as intramuscularly or intravenously (e.g. in the form of injection solutions), or topically, e.g. in the form of ointments, creams or oils.

The compounds of formula (I) and their pharmaceutically usable salts can be processed with pharmaceutically inert, inorganic or organic adjuvants for the production of tablets, coated tablets, dragées, and hard gelatine capsules. Lactose, corn starch or derivatives thereof, talc, stearic acid or its salts etc. can be used, for example, as such adjuvants for tablets, dragées, and hard gelatine capsules. Suitable adjuvants for soft gelatine capsules, are, for example, vegetable oils, waxes, fats, semi-solid substances and liquid polyols, etc. Suitable adjuvants for the production of solutions and syrups are, for example, water, polyols, saccharose, invert sugar, glucose, etc. Suitable adjuvants for injection solutions are, for example, water, alcohols, polyols, glycerol, vegetable oils, etc. Suitable adjuvants for suppositories are, for example, natural or hardened oils, waxes, fats, semi-solid or liquid polyols, etc.

Morever, the pharmaceutical preparations can contain preservatives, solubilizers, viscosity-increasing substances, stabilizers, wetting agents, emulsifiers, sweeteners, colorants, flavorants, salts for varying the osmotic pressure, buffers, masking agents or antioxidants. The compounds of formula (I) may also be used in combination with one or more other therapeutically useful substances. Examples are anorectic drugs like fenfluramine and related substances; lipase inhibitors like orlistat and related substances; antidepressants like fluoxetine and related substances; anxiolytics like alprazolam and

related substances; sleep-inducers like zopiclone and related substances; or any other therapeutically useful substance.

The dosage of compounds of formula (I) can vary within wide limits depending on the disease to be controlled, the age and the individual condition of the patient and the mode of administration, and will, of course, be fitted to the individual requirements in each particular case. For adult patients a daily dosage of about 1 mg to 1000 mg, especially about 50 mg to about 500 mg, comes into consideration.

The pharmaceutical preparations conveniently contain about 1 - 500 mg, preferably 5 - 200 mg of a compound of formula (I).

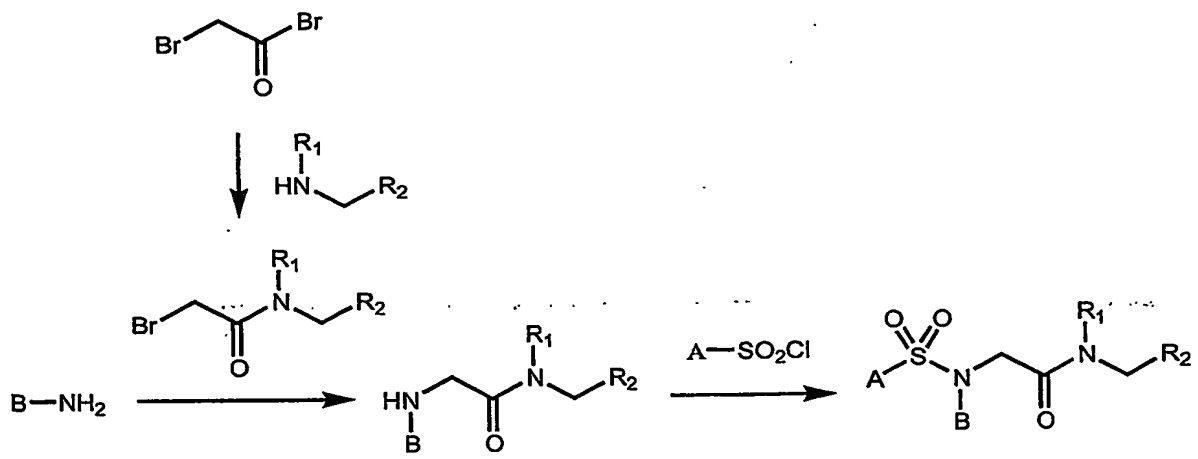
The compounds of general formula (I) of the present invention are prepared according to the general sequence of reactions outlined in the schemes below, wherein A, B, R^1, R^2 are as defined in formula (I) above. As the case may be any compound obtained with one or more optically active carbon atom may be resolved into pure enantiomers or diastereomers, mixtures of enantiomers or diastereomers, diastereomeric racemates and the meso-forms in a manner known per se.

The compounds obtained may also be converted into a pharmaceutically acceptable salt thereof in a manner known per se.

The compounds of formula (I) may be prepared as single compounds or as libraries of compounds comprising at least 2, typically 5 to 200 compounds of formula (I).

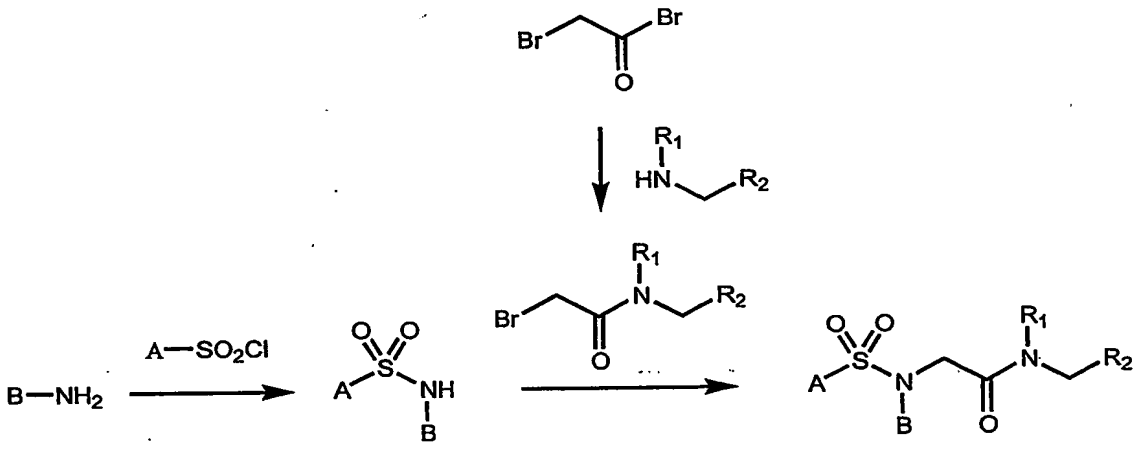
Compound libraries are prepared by multiple parallel synthesis using solution phase chemistry.

The compounds of formula (I) have been prepared by following one of two possible synthetic pathways. The first pathway starts with the reaction of an amine B-NH_2 with an α-bromoacetamide, which might be synthesised starting from bromoacetyl bromide and an amine $NHR^1(CH_2R^2)$ either *in situ* or separately. In a second step the respective aminoacetamide was reacted with a sulfonyl chloride A-SO_2Cl (*Scheme 1*).



Scheme 1

The second synthetic route starts with the reaction of an amine B-NH_2 with a sulfonyl chloride A-SO_2Cl. From the intermediate sulfonamides the target molecules can be obtained by reaction with the respective α-bromoacetamide (*Scheme 2*).



Scheme 2

Experimental Section

Abbreviations:

bp	Boiling point
BSA	Bovine serum albumine
CHO	Chinese hamster ovary
DCM	Dichloromethane
DMSO	Dimethylsulfoxide
ES	Electron spray
FCS	Foetal calf serum
FLIPR	Fluorescent imaging plate reader
h	Hour(s)
HBSS	Hank's balanced salt solution
HEPES	4-(2-Hydroxyethyl)-piperazine-1-ethanesulfonic acid
HPLC	High pressure/performance liquid chromatography
MS	Mass spectroscopy
LC	Liquid chromatography
min	Minute(s)
R_t	retention time
RT	Room temperature
THF	Tetrahydrofuran

I. Biology

Determination of Orexin receptor antagonistic activity

The Orexin receptor antagonistic activity of the compounds of formula (I) was determined in accordance with the following experimental method.

Experimental method:

Intracellular calcium measurements

Chinese hamster ovary (CHO) cells expressing the human orexin-1 receptor and the human orexin-2 receptor, respectively, were grown in culture medium (Ham F-12 with L-

Glutamine) containing 300 µg/ml G418, 100 U/ml penicillin, 100 µg/ml streptomycin and 10 % inactivated foetal calf serum (FCS).

The cells were seeded at 80'000 cells / well into 96-well black clear bottom sterile plates (Costar) which had been precoated with 1% gelatine in Hanks' Balanced Salt Solution (HBSS). All reagents were from Gibco BRL.

The seeded plates were incubated overnight at 37°C in 5% CO_2.

Human orexin-A as an agonist was prepared as 1 mM stock solution in methanol:water (1:1), diluted in HBSS containing 0.1 % bovine serum albumin (BSA) and 2 mM HEPES for use in the assay at a final concentration of 10 nM.

Antagonists were prepared as 10 mM stock solution in DMSO, then diluted in 96-well plates, first in DMSO, then in HBSS containing 0.1 % bovine serum albumin (BSA) and 2 mM HEPES.

On the day of the assay, 100 µl of loading medium (HBSS containing 1% FCS, 2 mM HEPES, 5 mM probenecid (Sigma) and 3 µM of the fluorescent calcium indicator fluo-3 AM (1 mM stock solution in DMSO with 10% pluronic acid) (Molecular Probes) was added to each well.

The 96-well plates were incubated for 60 min at 37° C in 5% CO_2. The loading solution was then aspirated and cells were washed 3 times with 200 µl HBSS containing 2.5 mM probenecid, 0.1% BSA, 2 mM HEPES. 100 µl of that same buffer was left in each well.

Within the Fluorescent Imaging Plate Reader (FLIPR, Molecular Devices), antagonists were added to the plate in a volume of 50 µl, incubated for 20 min and finally 100 µl of agonist was added. Fluorescence was measured for each well at 1 second intervals, and the height of each fluorescence peak was compared to the height of the fluorescence peak induced by 10 nM orexin-A with buffer in place of antagonist. For each antagonist, IC_{50} value (the concentration of compound needed to inhibit 50 % of the agonistic response) was determined. Selected compounds are displayed in *Table 1*.

	OX_1: IC_{50} [nM]	OX_2: IC_{50} [nM]
Example 2	>10000	14
Example 19	>10000	15
Example 22	>10000	12
Example 36	>5000	17
Example 37	>5000	12
Example 39	>10000	20
Example 41	1731	10
Example 44	898	5
Example 45	354	4
Example 47	>10000	15
Example 48	1189	9

Table 1

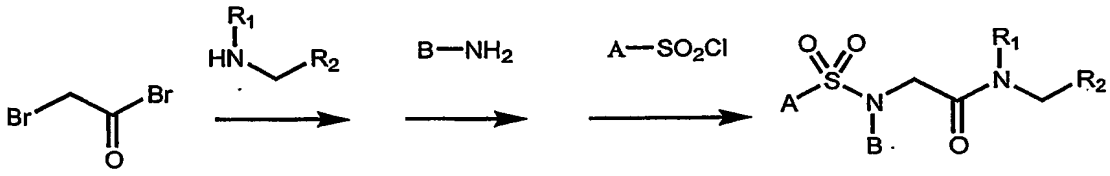
II. Chemistry

The following examples illustrate the preparation of pharmacologically active compounds of the invention but do not at all limit the scope thereof.

All temperatures are stated in °C.

All analytical and preparative HPLC investigations were performed using RP-C18 based columns.

A Synthesis of sulfonylamino-acetic acid derivatives via α-aminoacetamide intermediates (one-pot procedure)



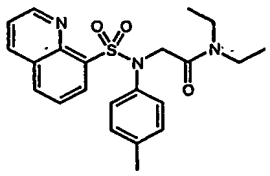
General Procedure:

A solution of 2-bromoacetyl bromide (0.30 mmol) in THF (0.50 mL) was cooled to 0°C and treated dropwise with the respective dialkylamine (0.30 mmol). After addition of ethyldiisopropylamine (1.80 mmol) the reaction mixture was allowed to reach RT and was stirred for 60 min. A solution of the primary amine B-NH_2 (0.30 mmol) in THF (0.50 mL) was added. The suspension was stirred at 60°C for 16 h, cooled to RT and treated with a solution of the respective sulfonyl chloride (0.30 mmol) in THF (0.50 mL). After 60 min the solvent was removed in vacuo

and the residue was purified by preparative HPLC chromatography to give the following sulfonamides:

Example 1:

***N,N*-Diethyl-2-[(quinoline-8-sulfonyl)-p-tolyl-amino]-acetamide:**

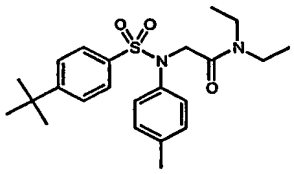


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 8-quinolinesulfonyl chloride

LC-MS: rt = 0.92 min, 412 (M+1, ES+).

Example 2:

2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide:

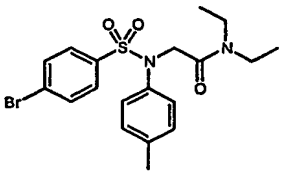


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.10 min, 417 (M+1, ES+).

Example 3:

2-[(4-Bromo-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide:

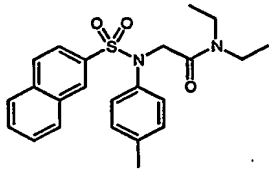


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 4-bromo-benzenesulfonyl chloride

LC-MS: rt = 1.04 min, 439 (M+1, ES+).

Example 4:

***N,N*-Diethyl-2-[(naphthalene-2-sulfonyl)-p-tolyl-amino]-acetamide:**

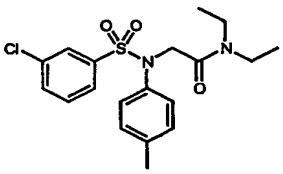


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 2-naphthalenesulfonyl chloride

LC-MS: rt = 1.04 min, 411 (M+1, ES+).

Example 5:

2-[(3-Chloro-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide:

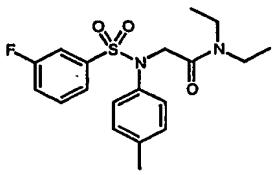


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 3-chloro-benzenesulfonyl chloride

LC-MS: rt = 1.02 min, 395 (M+1, ES+).

Example 6:

***N,N*-Diethyl-2-[(3-fluoro-benzenesulfonyl)-p-tolyl-amino]-acetamide:**

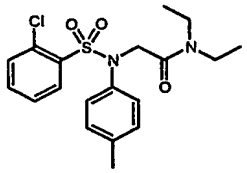


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 3-fluoro-benzenesulfonyl chloride

LC-MS: rt = 0.97 min, 379 (M+1, ES+).

Example 7:

2-[(2-Chloro-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide:

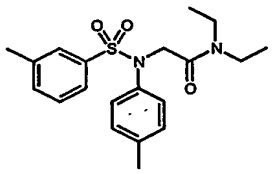


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 2-chloro-benzenesulfonyl chloride

LC-MS: rt = 0.98 min, 395 (M+1, ES+).

Example 8:

***N,N*-Diethyl-2-[(toluene-3-sulfonyl)-p-tolyl-amino]-acetamide:**

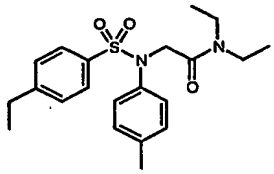


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and toluene-3-sulfonyl chloride

LC-MS: rt = 0.99 min, 375 (M+1, ES+).

Example 9:

***N,N*-Diethyl-2-[(4-ethyl-benzenesulfonyl)-p-tolyl-amino]-acetamide:**

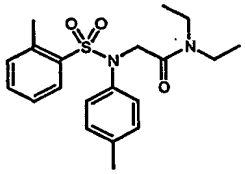


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 4-ethyl-benzenesulfonyl chloride

LC-MS: rt = 1.03 min, 389 (M+1, ES+).

Example 10:

***N,N*-Diethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide:**

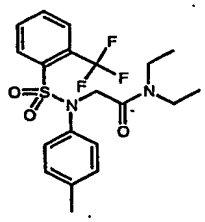


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and toluene-2-sulfonyl chloride

LC-MS: rt = 0.98 min, 375 (M+1, ES+).

Example 11:

***N,N*-Diethyl-2-[p-tolyl-(2-trifluoromethyl-benzenesulfonyl)-amino]-acetamide:**

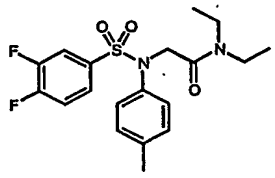


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 2-trifluoromethyl-benzenesulfonyl chloride

LC-MS: rt = 1.00 min, 429 (M+1, ES+).

Example 12:

2-[(3,4-Difluoro-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide:

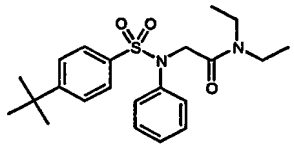


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-toluidine and 3,4-difluoro-benzenesulfonyl chloride

LC-MS: rt = 1.00 min, 397 (M+1, ES+).

Example 13:

2-[(4-tert-Butyl-benzenesulfonyl)-phenyl-amino]-*N,N*-diethyl-acetamide:

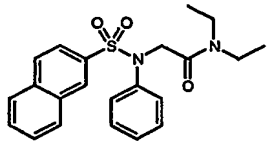


prepared by reaction of 2-bromoacetyl bromide with diethylamine, aniline and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.07 min, 403 (M+1, ES+).

Example 14:

***N,N*-Diethyl-2-[(naphthalene-2-sulfonyl)-phenyl-amino]-acetamide:**

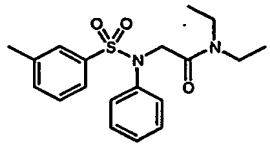


prepared by reaction of 2-bromoacetyl bromide with diethylamine, aniline and naphthalene-2-sulfonyl chloride

LC-MS: rt = 1.00 min, 397 (M+1, ES+).

Example 15:

***N,N*-Diethyl-2-[phenyl-(toluene-3-sulfonyl)-amino]-acetamide:**

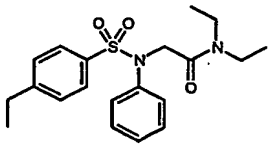


prepared by reaction of 2-bromoacetyl bromide with diethylamine, aniline and toluene-3-sulfonyl chloride

LC-MS: rt = 0.94 min, 361 (M+1, ES+).

Example 16:

***N,N*-Diethyl-2-[(4-ethyl-benzenesulfonyl)-phenyl-amino]-acetamide:**

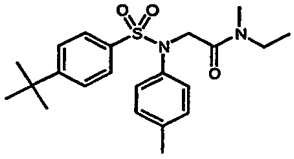


prepared by reaction of 2-bromoacetyl bromide with diethylamine, aniline and 4-ethyl-benzenesulfonyl chloride

LC-MS: rt = 0.99 min, 375 (M+1, ES+).

Example 17:

2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-methyl-acetamide:

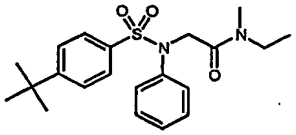


prepared by reaction of 2-bromoacetyl bromide with ethylmethylamine, *p*-toluidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.06 min, 403 (M+1, ES+).

Example 18:

2-[(4-tert-Butyl-benzenesulfonyl)-phenyl-amino]-*N*-ethyl-*N*-methyl-acetamide:

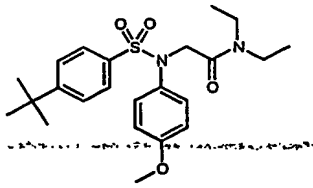


prepared by reaction of 2-bromoacetyl bromide with ethylmethylamine, aniline and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.02 min, 389 (M+1, ES+).

Example 19:

2-[(4-tert-Butyl-benzenesulfonyl)-(4-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide:

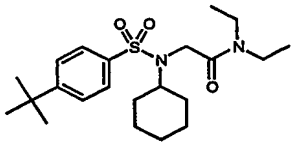


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *p*-anisidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.07 min, 433 (M+1, ES+).

Example 20:

2-[(4-tert-Butyl-benzenesulfonyl)-cyclohexyl-amino]-*N,N*-diethyl-acetamide:

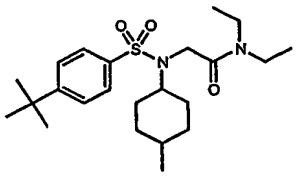


prepared by reaction of 2-bromoacetyl bromide with diethylamine, cyclohexyl-amine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.16 min, 409 (M+1, ES+).

Example 21:

2-[(4-tert-Butyl-benzenesulfonyl)-(4-methyl-cyclohexyl)-amino]-*N,N*-diethyl-acetamide:

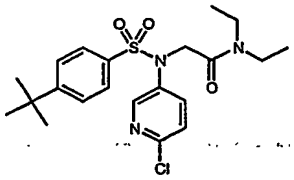


prepared by reaction of 2-bromoacetyl bromide with diethylamine, 4-methyl-cyclohexylamine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.20 min, 423 (M+1, ES+).

Example 22:

2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide:

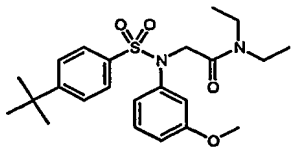


prepared by reaction of 2-bromoacetyl bromide with diethylamine, 5-amino-2-chloropyridine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.08 min, 438 (M+1, ES+).

Example 23:

2-[(4-tert-Butyl-benzenesulfonyl)-(3-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide:

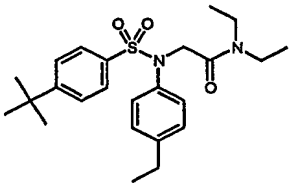


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *m*-anisidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.08 min, 433 (M+1, ES+).

Example 24:

2-[(4-tert-Butyl-benzenesulfonyl)-(4-ethyl-phenyl)-amino]-*N,N*-diethyl-acetamide:

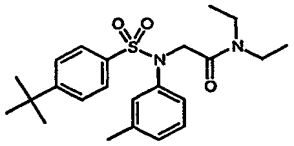


prepared by reaction of 2-bromoacetyl bromide with diethylamine, 4-ethylaniline and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.15 min, 431 (M+1, ES+).

Example 25:

2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N,N*-diethyl-acetamide:

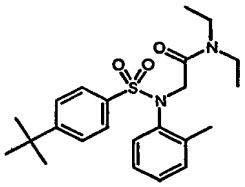


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *m*-toluidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.12 min, 417 (M+1, ES+).

Example 26:

2-[(4-tert-Butyl-benzenesulfonyl)-o-tolyl-amino]-*N,N*-diethyl-acetamide:

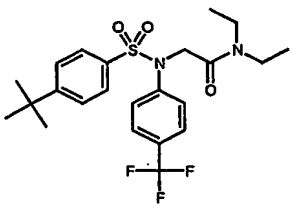


prepared by reaction of 2-bromoacetyl bromide with diethylamine, *o*-toluidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.12 min, 417 (M+1, ES+).

Example 27:

2-[(4-tert-Butyl-benzenesulfonyl)-(4-trifluoromethyl-phenyl)-amino]-*N,N*-diethyl-acetamide:

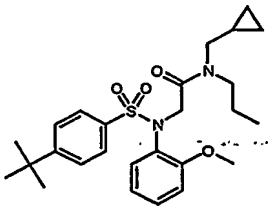


prepared by reaction of 2-bromoacetyl bromide with diethylamine, 4-trifluoromethyl-aniline and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.14 min, 471 (M+1, ES+).

Example 28:

2-[(4-tert-Butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-cyclopropyl-methyl-*N*-n-propyl-acetamide:

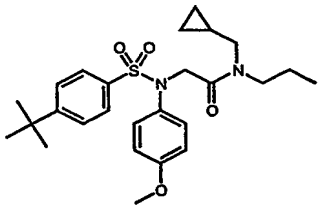


prepared by reaction of 2-bromoacetyl bromide with *N*-cyclopropylmethyl-*N*-propylamine, *o*-anisidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.17 min, 473 (M+1, ES+).

Example 29:

2-[(4-tert-Butyl-benzenesulfonyl)-(4-methoxy-phenyl)-amino]-*N*-cyclopropyl-methyl-*N*-n-propyl-acetamide:

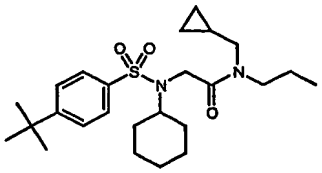


prepared by reaction of 2-bromoacetyl bromide with *N*-cyclopropylmethyl-*N*-propylamine, *p*-anisidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.16 min, 473 (M+1, ES+).

Example 30:

2-[(4-tert-Butyl-benzenesulfonyl)-cyclohexyl-amino]-*N*-cyclopropylmethyl-*N*-n-propyl-acetamide:

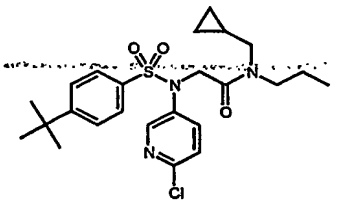


prepared by reaction of 2-bromoacetyl bromide with *N*-cyclopropylmethyl-*N*-propylamine, cyclohexylamine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.24 min, 449 (M+1, ES+).

Example 31:

2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N*-cyclopropylmethyl-*N*-n-propyl-acetamide:

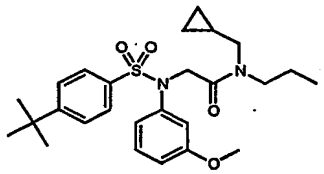


prepared by reaction of 2-bromoacetyl bromide with *N*-cyclopropylmethyl-*N*-propylamine, 5-amino-2-chloropyridine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.16 min, 478 (M+1, ES+).

Example 32:

2-[(4-tert-Butyl-benzenesulfonyl)-(3-methoxy-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-n-propyl-acetamide:

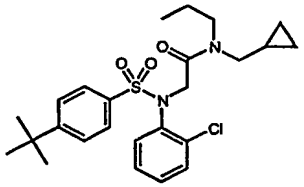


prepared by reaction of 2-bromoacetyl bromide with *N*-cyclopropylmethyl-*N*-propylamine, *m*-anisidine and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.17 min, 473 (M+1, ES+).

Example 33:

2-[(4-tert-Butyl-benzenesulfonyl)-(2-chloro-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-n-propyl-acetamide:

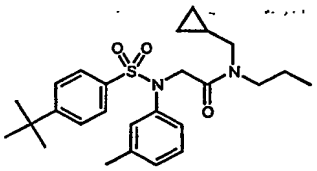


prepared by reaction of 2-bromoacetyl bromide with *N*-cyclopropylmethyl-*N*-propylamine, 2-chloroaniline and 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.21 min, 477 (M+1, ES+).

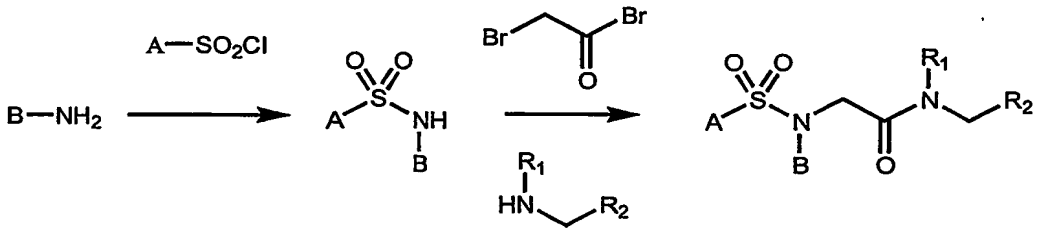
Example 34:

2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N*-cyclopropylmethyl-*N*-n-propyl-acetamide:



prepared by reaction of 2-bromoacetyl bromide with *N*-cyclopropylmethyl-*N*-propylamine, *m*-toluidine and 4-tert-butyl-benzenesulfonyl chloride
LC-MS: rt = 1.20 min, 457 (M+1, ES+).

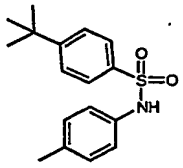
B Synthesis of sulfonylamino-acetic acid derivatives via isolated sulfanilide-intermediates (two step procedure)



B.1 Synthesis of sulfanilide-intermediates (general procedure):

The respective sulfonyl chloride (100 mmol) was added portionwise to a solution of the respective aromatic amine (100 mmol) and ethyldiisopropylamine (120 mmol) in THF (100 mL) at RT. The suspension was stirred for 16 h, the solvent was removed in vacuo and the residue was redissolved in ethyl acetate. After washing the organic phase with water and brine the solvent was removed in vacuo. The residue was purified by crystallization from diethylether to give the following sulfonamides:

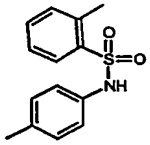
4-tert-Butyl-*N*-p-tolyl-benzenesulfonamide:



prepared by reaction of *p*-toluidine with 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.18 min, 304 (M+1, ES+).

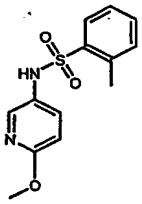
2-Methyl-*N*-p-tolyl-benzenesulfonamide:



prepared by reaction of *p*-toluidine with 2-methyl-benzenesulfonyl chloride

LC-MS: rt = 1.06 min, 523 (2M+1, ES+).

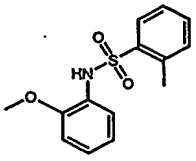
***N*-(6-Methoxy-pyridin-3-yl)-2-methyl-benzenesulfonamide:**



prepared by reaction of 6-methoxy-pyridin-3-ylamine with 2-methyl-benzenesulfonyl chloride

LC-MS: rt = 0.85 min, 279 (M+1, ES+).

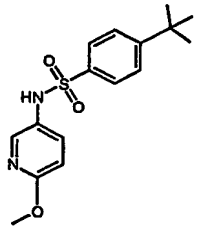
***N*-(2-Methoxy-phenyl)-2-methyl-benzenesulfonamide:**



prepared by reaction of *o*-anisidine with 2-methyl-benzenesulfonyl chloride

LC-MS: rt = 0.93 min, 278 (M+1, ES+).

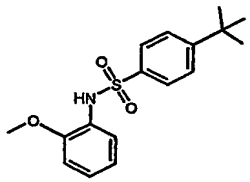
4-tert-Butyl-*N*-(6-methoxy-pyridin-3-yl)-benzenesulfonamide:



prepared by reaction of 6-methoxy-pyridin-3-ylamine with 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 0.96 min, 321 (M+1, ES+).

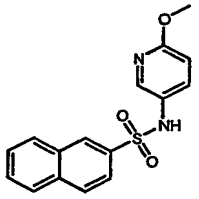
4-tert-Butyl-*N*-(2-methoxy-phenyl)-benzenesulfonamide:



prepared by reaction of *o*-anisidine with 4-tert-butyl-benzenesulfonyl chloride

LC-MS: rt = 1.02 min, 320 (M+1, ES+).

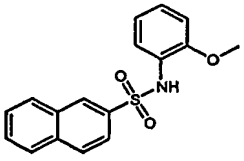
Naphthalene-2-sulfonic acid (6-methoxy-pyridin-3-yl)-amide:



prepared by reaction of 6-methoxy-pyridin-3-ylamine with naphthalene-2-sulfonyl chloride

LC-MS: rt = 0.91 min, 315 (M+1, ES+).

Naphthalene-2-sulfonic acid (2-methoxy-phenyl)-amide:



prepared by reaction of *o*-anisidine with naphthalene-2-sulfonyl chloride

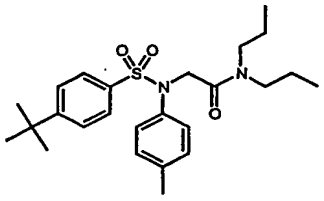
LC-MS: rt = 0.97 min, 314 (M+1, ES+).

B.2 Synthesis of sulfonylamino-acetic acid derivatives (general procedure):

To a solution of 2-bromoacetyl bromide (0.20 mmol) in THF (1.0 mL) was added a solution of the respective amine (0.20 mmol) in THF (0.50 mL) at RT. A solution of potassium tert-butoxide (0.20 mmol) in THF (0.50 mL) was added and the reaction mixture was stirred for 2 h. To this suspension a solution of the respective potassium *N*-tolylsulfonamide was added, which was obtained by adding potassium tert-butoxide (0.20 mmol) to a solution of the respective sulfonamide (0.20 mmol) in THF (2.5 mL) and diluting with DMSO (0.50 mL). The obtained suspension was stirred at 60°C for 1 h, the solvent was removed in vacuo and the residue was purified by preparative HPLC chromatography to give the following sulfonamides:

Example 35:

2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*,*N*-di-n-propyl-acetamide:

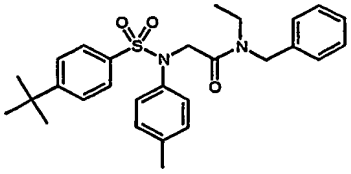


prepared by reaction of 2-bromoacetyl bromide with di-n-propylamine and 4-tert-butyl-*N*-p-tolyl-benzenesulfonamide

LC-MS: rt = 1.20 min, 445 (M+1, ES+).

Example 36:

***N*-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-acetamide:**

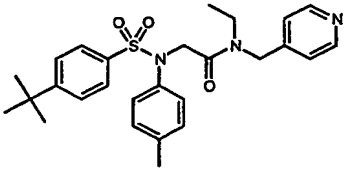


prepared by reaction of 2-bromoacetyl bromide with *N*-benzyl-*N*-ethylamine and 4-tert-butyl-*N*-p-tolyl-benzenesulfonamide

LC-MS: rt = 1.19 min, 479 (M+1, ES+).

Example 37:

2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-pyridin-4-ylmethyl-acetamide:

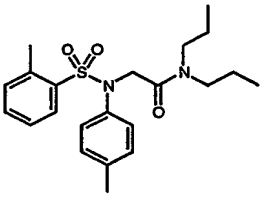


prepared by reaction of 2-bromoacetyl bromide with *N*-ethyl-*N*-pyridin-4-ylmethylamine and 4-tert-butyl-*N*-p-tolyl-benzenesulfonamide

LC-MS: rt = 0.83 min, 480 (M+1, ES+).

Example 38:

***N,N*-Di-n-propyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide:**

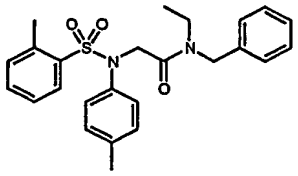


prepared by reaction of 2-bromoacetyl bromide with di-n-propylamine and 2-methyl-*N*-p-tolyl-benzenesulfonamide

LC-MS: rt = 1.20 min, 403 (M+1, ES+).

Example 39:

***N*-Benzyl-*N*-ethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide:**

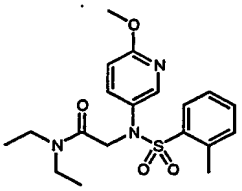


prepared by reaction of 2-bromoacetyl bromide with *N*-benzyl-*N*-ethylamine and 2-methyl-*N*-p-tolyl-benzenesulfonamide

LC-MS: rt = 1.20 min, 437 (M+1, ES+).

Example 40:

***N,N*-Diethyl-2-[(6-methoxy-pyridin-3-yl)-(toluene-2-sulfonyl)-amino]-acetamide:**

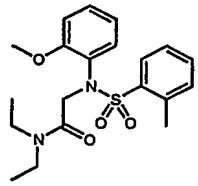


prepared by reaction of 2-bromoacetyl bromide with diethylamine and *N*-(6-methoxy-pyridin-3-yl)-2-methyl-benzenesulfonamide

LC-MS: rt = 0.93 min, 392 (M+1, ES+).

Example 41:

***N,N*-Diethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide:**

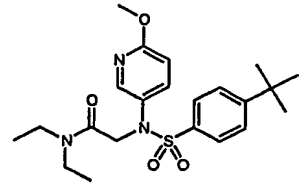


prepared by reaction of 2-bromoacetyl bromide with diethylamine and *N*-(2-methoxy-phenyl)-2-methyl-benzenesulfonamide

LC-MS: rt = 0.96 min, 391 (M+1, ES+).

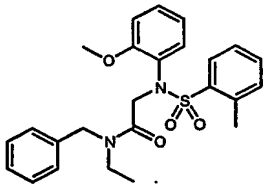
Example 42:

2-[(4-tert-Butyl-benzenesulfonyl)-(6-methoxy-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide:



Example 45:

***N*-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide:**

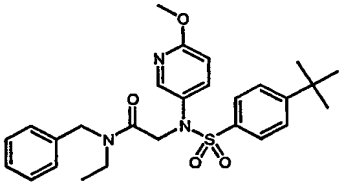


prepared by reaction of 2-bromoacetyl bromide with *N*-benzyl-*N*-ethylamine and *N*-(2-methoxy-phenyl)-2-methyl-benzenesulfonamide

LC-MS: rt = 1.04 min, 453 (M+1, ES+).

Example 46:

***N*-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-(6-methoxy-pyridin-3-yl)-amino]-*N*-ethyl-acetamide:**

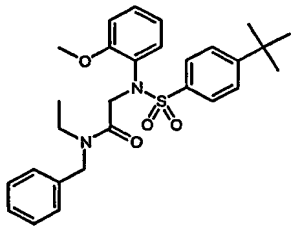


prepared by reaction of 2-bromoacetyl bromide with *N*-benzyl-*N*-ethylamine and 4-tert-butyl-*N*-(6-methoxy-pyridin-3-yl)-benzenesulfonamide

LC-MS: rt = 1.08 min, 496 (M+1, ES+).

Example 47:

***N*-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-ethyl-acetamide:**

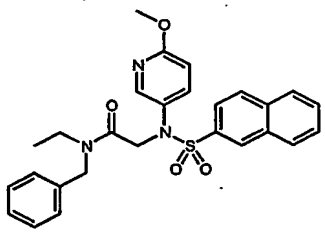


prepared by reaction of 2-bromoacetyl bromide with *N*-benzyl-*N*-ethylamine and 4-tert-butyl-*N*-(2-methoxy-phenyl)-benzenesulfonamide

LC-MS: rt = 1.10 min, 495 (M+1, ES+).

Example 48:

***N*-Benzyl-*N*-ethyl-2-[(6-methoxy-pyridin-3-yl)-(naphthalene-2-sulfonyl)-amino]-acetamide:**

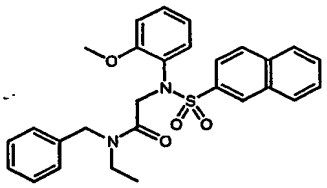


prepared by reaction of 2-bromoacetyl bromide with *N*-benzyl-*N*-ethylamine and naphthalene-2-sulfonic acid (6-methoxy-pyridin-3-yl)-amide

LC-MS: rt = 1.05 min, 490 (M+1, ES+).

Example 49:

***N*-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(naphthalene-2-sulfonyl)-amino]-acetamide:**

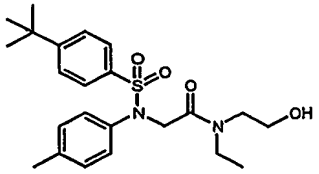


prepared by reaction of 2-bromoacetyl bromide with *N*-benzyl-*N*-ethylamine and naphthalene-2-sulfonic acid (2-methoxy-phenyl)-amide

LC-MS: rt = 1.06 min, 489 (M+1, ES+).

Example 50:

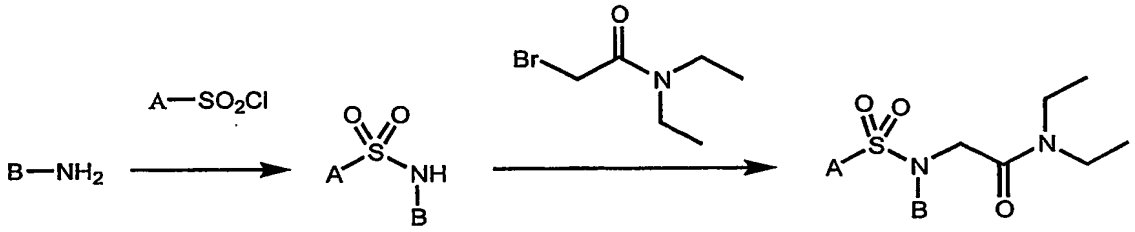
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-(2-hydroxy-ethyl)-acetamide:



prepared by reaction of 2-bromoacetyl bromide with *N*-ethyl-*N*-(2-hydroxy-ethyl)-amine and 4-tert-butyl-*N*-p-tolyl-benzenesulfonamide; in contrast to the general

procedure the intermediate 2-bromo-*N*-ethyl-*N*-(2-hydroxy-ethyl)-acetamide was isolated before being used in the coupling with the potassium *N*-tolylsulfonamide. LC-MS: rt = 0.97 min, 433 (M+1, ES+).

C Synthesis of sulfonylamino-acetic acid derivatives via isolated 2-bromo-*N,N*-diethylacetamide (two step procedure)



C.1 Synthesis of 2-bromo-*N,N*-diethylacetamide :

A solution of 2-bromoacetyl bromide (20.2 g, 100 mmol) in THF (300 mL) was cooled to 0°C and treated with diethylamine (7.31 g, 100 mmol). After dropwise addition of ethyldiisopropylamine (15.5 g, 120 mmol) the reaction mixture was allowed to reach RT and was stirred for 90 min. Water (250 mL) and ethyl acetate (300 mL) were added, the layers were separated and the aqueous layer was extracted twice with ethyl acetate (100 mL). The solvents were removed in vacuo and the residue was purified by destillation (bp 120 - 121°C / 24 mbar) to give 5.24 g (27%) of the title compound as pale yellow oil.

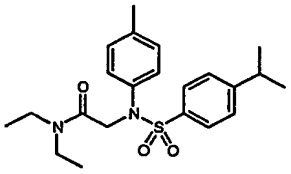
C.2 Synthesis of sulfonylamino-acetic acid derivatives (general procedure):

A solution of the respective sulfonyl chloride (0.20 mmol) in DCM (1.0 mL) was added to a solution of *p*-toluidine (0.20 mmol) and ethyldiisopropylamine (0.24 mmol) in DCM (1.0 mL) at RT. After stirring for 16 h water was added, the layers were separated and the aqueous layer was extracted twice with DCM (2.0 mL). The combined organic extracts were concentrated in vacuo and dissolved in dry THF (1.0 mL). A solution of potassium tert-butoxide (0.20 mmol) in THF (0.50 mL) was added. The reaction mixture was treated with a solution of 2-bromo-*N,N*-diethylacetamide (0.20 mmol) in THF (0.50 mL) and stirred for 16 h at RT. The

solvent was removed in vacuo and the residue was purified by preparative HPLC chromatography to give the following sulfonamides:

Example 51:

***N,N*-Diethyl-2-[(4-isopropyl-benzenesulfonyl)-p-tolyl-amino]-acetamide:**

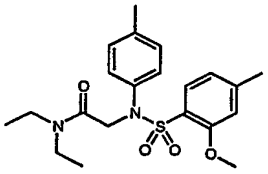


prepared by reaction of 2-bromo-*N,N*-diethylacetamide with *p*-toluidine and 4-isopropyl-benzenesulfonyl chloride

LC-MS: rt = 1.04 min, 403 (M+1, ES+).

Example 52:

***N,N*-Diethyl-2-[(2-methoxy-4-methyl-benzenesulfonyl)-p-tolyl-amino]-acetamide:**

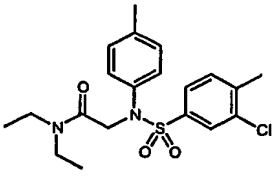


prepared by reaction of 2-bromo-*N,N*-diethylacetamide with *p*-toluidine and 2-methoxy-4-methyl-benzenesulfonyl chloride

LC-MS: rt = 0.96 min, 405 (M+1, ES+).

Example 53:

2-[(3-Chloro-4-methyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide:

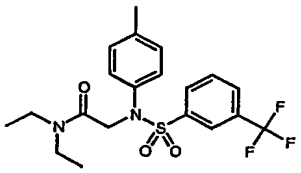


prepared by reaction of 2-bromo-*N,N*-diethylacetamide with *p*-toluidine and 3-chloro-4-methyl-benzenesulfonyl chloride

LC-MS: rt = 1.03 min, 409 (M+1, ES+).

Example 54:

***N,N*-Diethyl-2-[p-tolyl-(3-trifluoromethyl-benzenesulfonyl)-amino]-acetamide:**

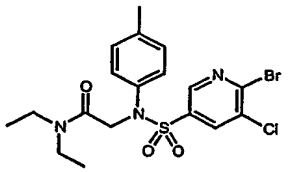


prepared by reaction of 2-bromo-*N,N*-diethylacetamide with *p*-toluidine and 3-trifluoromethyl-benzenesulfonyl chloride

LC-MS: rt = 1.03 min, 429 (M+1, ES+).

Example 55:

2-[(6-Bromo-5-chloro-pyridine-3-sulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide:

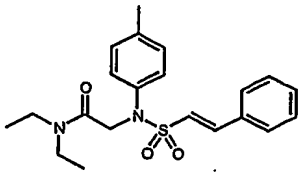


prepared by reaction of 2-bromo-*N,N*-diethylacetamide with *p*-toluidine and 6-bromo-5-chloro-pyridine-3-sulfonyl chloride

LC-MS: rt = 1.04 min, 474 (M+1, ES+).

Example 56:

***N,N*-Diethyl-2-[((E)-2-phenyl-ethenesulfonyl)-p-tolyl-amino]-acetamide:**

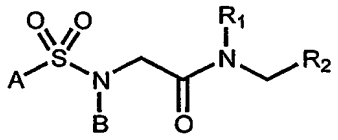


prepared by reaction of 2-bromo-*N,N*-diethylacetamide with *p*-toluidine and (E)-2-phenyl-ethenesulfonyl chloride

LC-MS: rt = 1.01 min, 387 (M+1, ES+).

Claims

1. Compounds of formula (I)



Formula (I)

wherein:

A represents 4-ethylphenyl-, 4-isopropylphenyl-, 4-*tert.*-butylphenyl-, 2-methylphenyl-, 3-methylphenyl-, 3-fluorophenyl-, 2-chlorophenyl-, 3-chlorophenyl-, 4-bromophenyl-, 2-trifluoromethylphenyl-, 3-trifluoromethylphenyl-, 3-chloro-4-methylphenyl-, 2-methoxy-4-methylphenyl-, 3,4-difluorophenyl-, phenylethenyl-, 1-naphthyl-, 2-naphthyl-, 6-bromo-5-chloro-pyridin-3-yl or 8-quinolinyl-;

B represents a phenyl or 6-membered heteroaryl group, which groups are unsubstituted or independently mon- or di-substituted with cyano, halogen, hydroxy, lower alkyl, hydroxy lower alkyl, amino lower alkyl, aminocarbonyl lower alkyl, sulfonylamino lower alkyl, lower alkenyl, lower alkoxy, trifluoromethyl, trifluoromethoxy, cycloalkyloxy, aryloxy, aralkyloxy, heterocyclyloxy, heterocyclyl lower alkyloxy, amino, aminocarbonyl or sulfonylamino; or a cyclohexyl, 3-piperidinyl or 4-piperidinyl group, which groups are unsubstituted or mono-substituted with hydroxy, lower alkyl, hydroxy lower alkyl, aminocarbonyl lower alkyl, sulfonylamino lower alkyl, amino, aminocarbonyl or sulfonylamino;

with the proviso that in case A represents 2-methylphenyl- or 4-bromophenyl the phenyl ring as represented by B is substituted;

R^1 represents lower alkyl;

R^2 represents lower alkyl, lower alkenyl, hydroxy lower alkyl, amino lower alkyl, sulfonylamino lower alkyl, cycloalkyl; an unsubstituted or mono- or di-substituted phenyl group substituted independently with cyano, halogen, hydroxy, lower alkyl, lower alkoxy, cycloalkyloxy, amino, aminocarbonyl or sulfonylamino; an unsubstituted or mono- or di-substituted five- or six-membered heteroaryl group substituted independently with cyano, halogen, hydroxy, lower alkyl, lower alkoxy, cycloalkyloxy, amino, aminocarbonyl or sulfonylamino;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

2. Compounds of formula (I) wherein:

A represents a 4-ethylphenyl group;

B, R^1 and R^2 have the meaning given in claim 1;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

3. Compounds of formula (I) wherein:

A represents a 4-isopropylphenyl group;

B, R^1 and R^2 have the meaning given in claim 1;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

4. Compounds of formula (I) wherein:

A represents a 4-*tert.*-butylphenyl group;

B, R^1 and R^2 have the meaning given in claim 1;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

5. Compounds of formula (I) wherein:

A represents a 2-methylphenyl group;

B has the meaning given in claim 1 with the proviso that the phenyl group is substituted;

R^1 and R^2 have the meaning given in claim 1;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

6. Compounds of formula (I) wherein:

A represents a 3-methylphenyl group;

B, R^1 and R^2 have the meaning given in claim 1;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

7. Compounds of formula (I) wherein:

A represents a 3-chloro-4-methylphenyl group;

B, R^1 and R^2 have the meaning given in claim 1;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

8. Compounds of formula (I) wherein:

A represents a 2-naphthyl group;

B, R^1 and R^2 have the meaning given in claim 1;

and pure enantiomers, mixtures of enantiomers, pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates and the meso-form and pharmaceutically acceptable salts, solvent complexes, and morphological forms thereof.

9. A compound according to any of claims 1 to 8, selected from the group consisting of

N,N-Diethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide;

N,N-Diethyl-2-[(toluene-3-sulfonyl)-p-tolyl-amino]-acetamide;

N,N-Diethyl-2-[(4-ethyl-benzenesulfonyl)-p-tolyl-amino]-acetamide;

N,N-Diethyl-2-[(4-isopropyl-benzenesulfonyl)-p-tolyl-amino]-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-phenyl-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-cyclohexyl-amino]-*N,N*-diethyl-acetamide;

2-[(3-Chloro-4-methyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;

N,N-Diethyl-2-[(naphthalene-2-sulfonyl)-p-tolyl-amino]-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-o-tolyl-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;

2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-methyl-cyclohexyl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(3-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(4-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
N-Benzyl-*N*-ethyl-2-[(toluene-2-sulfonyl)-p-tolyl-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N,N*-dipropyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-m-tolyl-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(6-chloro-pyridin-3-yl)-amino]-*N*-cyclopropylmethyl-*N*-propyl-acetamide;
N-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-p-tolyl-amino]-*N*-ethyl-*N*-pyridin-4-ylmethyl-acetamide;
N,N-Diethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(6-methoxy-pyridin-3-yl)-amino]-*N,N*-diethyl-acetamide;
2-[(4-tert-Butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N,N*-diethyl-acetamide;
N-Benzyl-*N*-ethyl-2-[(6-methoxy-pyridin-3-yl)-(toluene-2-sulfonyl)-amino]-acetamide;
N-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(toluene-2-sulfonyl)-amino]-acetamide;
N-Benzyl-2-[(4-tert-butyl-benzenesulfonyl)-(2-methoxy-phenyl)-amino]-*N*-ethyl-acetamide;
N-Benzyl-*N*-ethyl-2-[(6-methoxy-pyridin-3-yl)-(naphthalene-2-sulfonyl)-amino]-acetamide;
N-Benzyl-*N*-ethyl-2-[(2-methoxy-phenyl)-(naphthalene-2-sulfonyl)-amino]-acetamide.

10. Pharmaceutical compositions for the treatment of disorders which are associated with the role of orexin, comprising one or more compounds of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, and usual carrier materials and adjuvants.